

## Enhanced differentiation of human neural crest stem cells towards the Schwann cell lineage by aligned electrospun fiber matrix.

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### Public Summary:

Human pluripotent stem cell-derived neural crest stem cells (NCSCs) provide a promising cell source for generating Schwann cells in the treatment of neurodegenerative diseases and traumatic injuries in the peripheral nervous system. Influencing cell behavior through a synthetic matrix topography has been shown to be an effective approach to directing stem cell proliferation and differentiation. Here we have investigated the effect of nanofiber topography on the differentiation of human embryonic stem cell-derived NCSCs towards the Schwann cell lineage. Using electrospun fibers of different diameters and alignments we demonstrated that aligned fiber matrices effectively induced cell alignment, and that fiber matrices with average diameters of 600nm and 1.6µm most effectively promoted NCSC differentiation towards the Schwann cell lineage compared with random fibers and two-dimensional tissue culture plates. More importantly, human NCSCs that were predifferentiated in Schwann cell medium for 2weeks exhibited higher sensitivity to the aligned fiber topography than undifferentiated NCSCs. This study provides an efficient protocol for Schwann cell derivation by combining an aligned nanofiber matrix and an optimized differentiation medium, and highlights the importance of matching extrinsic matrix signaling with cell intrinsic programming in a temporally specific manner.

### Scientific Abstract:

Human pluripotent stem cell-derived neural crest stem cells (NCSCs) provide a promising cell source for generating Schwann cells in the treatment of neurodegenerative diseases and traumatic injuries in the peripheral nervous system. Influencing cell behavior through a synthetic matrix topography has been shown to be an effective approach to directing stem cell proliferation and differentiation. Here we have investigated the effect of nanofiber topography on the differentiation of human embryonic stem cell-derived NCSCs towards the Schwann cell lineage. Using electrospun fibers of different diameters and alignments we demonstrated that aligned fiber matrices effectively induced cell alignment, and that fiber matrices with average diameters of 600nm and 1.6µm most effectively promoted NCSC differentiation towards the Schwann cell lineage compared with random fibers and two-dimensional tissue culture plates. More importantly, human NCSCs that were predifferentiated in Schwann cell medium for 2weeks exhibited higher sensitivity to the aligned fiber topography than undifferentiated NCSCs. This study provides an efficient protocol for Schwann cell derivation by combining an aligned nanofiber matrix and an optimized differentiation medium, and highlights the importance of matching extrinsic matrix signaling with cell intrinsic programming in a temporally specific manner.

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